National Centers for Biomedical Computing

RFA Number: RFA-RM-04-022

Part I Overview Information

Department of Health and Human Services

Participating Organization:
National Institutes of Health (NIH), (http://www.nih.gov)

Components of Participating Organizations:
This RFA is developed as a Roadmap initiative. All NIH Institutes and Centers participate in Roadmap initiatives.

Announcement Type:
This is a reissue of RFA-RM-04-003 which was previously released on September 29, 2003.

Catalog of Federal Domestic Assistance Number(s): 93.859

Key Dates

Release Date: September 28, 2004
Technical Assistance Workshop: October 28, 2004
Letters Of Intent Receipt Date(s): December 20, 2004
Application Receipt Dates(s): January 24, 2005
Peer Review Date(s): April-June 2005
Council Review Date(s) : August-September 2005
Earliest Anticipated Start Date: September 15, 2005
Expiration Date: January 25, 2005

Due Dates for E.O. 12372 Not Applicable

Executive Summary
Participating Institutes and Centers (ICs) of the National Institutes of Health under the Roadmap initiative invite applications for specialized Centers in the area of biomedical computing. The U54 cooperative agreement mechanism will be used to create the NIH National Centers for Biomedical Computing (NCBC). These Centers, in conjunction with individual investigator awards, will create a networked national effort to build the computational infrastructure for biomedical computing in the nation, the National Program of Excellence in Biomedical Computing (NPEBC). The NIH NCBC will be devoted to all facets of biomedical computing, from basic research in computational science to providing the tools and resources that biomedical and behavioral researchers need to do their work. In addition to carrying out fundamental research, it is expected that the NIH NCBC will play a major role in educating and training researchers to engage in biomedical computing. In this second competition for the NCBC, the NIH intends to commit $12-14 million dollars in FY 2005 to fund three new Centers. Eligible organizations include domestic public or private institutions, units of State and local governments, and eligible agencies of the Federal government. For-profit organizations are not eligible to apply for a Center, but partnerships are welcome. Foreign institutions are not eligible to apply for a Center, but foreign institutions can participate as subcontractors in any of the Cores. There is no limit on the number of applications from an institution or individual. Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic

groups as well as individuals with disabilities are always encouraged to apply for NIH programs. The Principal Investigator of each Center must devote at least 25% of his/her effort. There will be a Technical Assistance Workshop on October 28, 2004. The PHS 398 application instructions are available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov. Telecommunications for the hearing impaired: TTY 301-451-0088.

This RFA will be administered by the National Institute of General Medical Sciences (NIGMS).

Table of Contents

Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

Purpose of this RFA:

Participating Institutes and Centers (ICs) of the National Institutes of Health under the Roadmap initiative invite applications for specialized Centers in the area of biomedical computing. The U54 mechanism will be used to create NIH National Centers for Biomedical Computing (NCBC). These Centers, in conjunction with individual investigator awards, will create a networked national effort to build the computational infrastructure for biomedical computing in the nation, the National Program of Excellence in Biomedical Computing (NPEBC). The establishment of the NIH NCBC was called for in the Biomedical Information Science and Technology Initiative (BISTI) report in 1999 (http://www.nih.gov/about/director/060399.htm), and the need has been reaffirmed by participants at more recent workshops. The NIH NCBC will be devoted to all facets of biomedical computing, from basic research in computational science to providing the tools and resources that biomedical and behavioral researchers need to do their work. In addition to carrying out fundamental research, it is expected that the NIH NCBC will play a major role in educating and training researchers to engage in biomedical computing.

To build the computational infrastructure for biomedical computing in the nation, the NPEBC will use a combination of NIH funding mechanisms that will be supported by multiple NIH Institutes and Centers. The central constituent of the NPEBC, the NIH NCBC, is the focus of this RFA. This is the second competition for the NIH NCBC. Information on the 2004 awarded NIH NCBC can be found at http://www.bisti.nih.gov/ncbc. The NIH NCBC will develop and provide tools and resources that biomedical and behavioral researchers can use at a variety of levels.

The NIH NCBC will be partnerships bringing together three types of scientists: 1) computational scientists, who invent and develop efficient and powerful languages, data structures, software architectures, hardware, and algorithms for solving biomedically significant computing problems; 2) biomedical computational scientists, who adapt and deploy resources from computational science to solve significant biomedical problems; and 3) experimental and clinical biomedical and behavioral researchers, who work on problems that can be transformed by computational biology. These partnerships will be designed to produce, validate, and disseminate tools and computational environments that will be useful to a broad spectrum of biomedical researchers across the nation. It is expected that the partnerships will be highly interactive and will form a loop. Computational scientists will work with experimental and clinical biomedical and behavioral researchers to develop the tools while those researchers will validate the tools and provide feedback for the next generation of tools. It is not expected that the biomedical and behavioral researchers will simply measure data and then turn it over to the computational group for analysis. The Driving Biological Projects (DBPs) will be the main method used by these Centers to drive the collaboration across disciplines. In some cases, NIH

NCBC Centers will enhance and extend existing tools; in other cases they will develop new tools and computational environments de novo.

The NIH NCBC will be national in scope and function as evidenced by the DBPs, dissemination efforts, training, and potential for future collaborations.

Individual biomedical or behavioral investigators will make use of the NIH NCBC in different ways. Some investigators will simply use the on-line tools and services that the NIH NCBC provide. These investigators might never have direct contact with any researchers at an NIH NCBC Center, but they will download software or go to a Center's web site to make use of resources found there.

Biomedical and behavioral investigators, for whom a greater level of interaction with the NIH NCBC is appropriate, could follow two pathways.

1. NIH anticipates releasing a program announcement that will support partnerships between individual investigators and the NIH NCBC. As an example, a biomedical research laboratory with software that is useful in modeling the function of the heart might seek to use the expertise of a Center to modify the software to run on a computational grid. Alternatively, the biomedical researchers might seek support from a Center to design and build hardware that would be well suited to solve their problems. Individual investigators should monitor the BISTI web site (http://www.bisti.nih.gov) for relevant program announcements. It is anticipated that the announcements for partnering projects will include both new R01s and R21s and as well as competitively reviewed supplements to existing projects.
2. Individual investigators could be part of a DBP funded within a Center. These projects will be described in Core 3 below. An investigator who interacts with a Center in this fashion will help to focus its computational research on challenging biomedical problems selected for their broad biomedical significance and compatibility with the core computational expertise of the Center. Investigators involved in a DBP will have substantial interactions with researchers at a Center.

NIH staff will conduct one technical assistance and information-sharing workshop in Bethesda, MD on October 28, 2004. This workshop will allow applicants and NIH staff to discuss and clarify any issues or questions related to this RFA. If you plan to attend the workshop, please contact Mr. Kevin Lauderdale (e-mail lauderdk@nigms.nih.gov or phone 301-451-6446) to reserve a space. Detailed information about the time and location of the meeting will be available at the BISTI web site http://www.bisti.nih.gov. To accommodate individuals who cannot attend the meeting, provisions will be made to distribute the information discussed. These provisions will also be posted on the BISTI web site.

Research Objectives:

Increasingly, the most exciting science and the most fruitful scientific and technical approaches to biomedical and behavioral research require approaches that involve bioinformatics and computational biology as well as experimentation. To meet the infrastructure needs of modern biomedical and behavioral research, the NIH is embarking on a long-term initiative aimed at deploying an integrated national biomedical computing environment. This environment will enable the analysis, modeling, understanding, and prediction of dynamic and complex biomedical systems across time and distance scales and will allow the integration of biomedical and behavioral data and knowledge at all levels of organization. All applications in response to this announcement will be evaluated primarily for the potential of the proposed activities to contribute to this long-term goal.

This RFA provides for the establishment of NIH-supported NCBC in the service of this long-term initiative. The NIH NCBC will be charged with core responsibilities in implementing and coordinating a national project to develop, improve, and integrate components of biomedical computing. For example, a particular Center could focus on algorithms, software development and engineering, modeling and methods of validation, definition of hardware requirements, and user interface

development to provide an excellent computational environment for one or more classes of biomedically important computing, such as:

- Comparative genomics
- Biomolecular modeling and simulation
- Analysis and modeling based on high throughput experimental techniques
- Image analysis, reconstruction, and validation methods
- Heterogeneous data integration
- Clinical trial management
- Epidemiological analysis and modeling
- Use of biomimetic principles in device design
- Multiscale modeling and simulation of biological processes
- Computational and information frameworks for integrating biological and behavioral data

Examples of computational environments that might ultimately be created could include:

- A graphical user interface (GUI)-enabled environment that would integrate homology and motif search tools, phylogenetic profiling, proteomics and microarray analysis, and intelligent text-mining to identify gene function and networks of interacting gene products.
- An environment that would integrate molecular modeling and simulation tools including homology-based structural modeling, electronic structure calculations, classical molecular dynamics and Monte Carlo sampling, electrostatics, molecular docking, and stochastic dynamics, to provide the best possible inference of structure-function relationships in biomolecules.
- A GUI-enabled environment that would integrate sequence analysis, traditional and high-throughput cell and molecular biology data analysis, clinical and behavioral data analysis, and intelligent text data mining, to understand the significance of single-nucleotide polymorphisms in determining varied response of individual patient responses to clinical interventions.
- A software development and dissemination environment, or software framework, that would enable concurrent developer access to a moderated repository for the purpose of multi-scale organ modeling. Such an environment would allow a geographically diverse team to work on a significant biomedical problem.

The above lists are intended to be exemplary rather than exhaustive or prescriptive.

The environments should be constructed by considering the entire range of computational techniques that apply to a particular biomedical issue. In these environments all the relevant computational techniques will be embodied in components that are robust, efficient, easy to use, widely disseminated, interoperable, versatile, in conformity with best practices in software engineering, and well tuned to the most appropriate and powerful free-standing hardware and grid computing environments. Applicants for an NIH NCBC Center are encouraged to consider similar far-reaching scenarios, as a guide to long-term goals for the NIH NCBC. Although the NIH NCBC as a whole will be aimed at solving a large, long-term problem, each individual Center will be focused on solving smaller problems in a five to ten-year time frame.

Organizational Structure of the NIH NCBC:

Each NIH NCBC Center will be required to perform or facilitate seven different Core functions: (1) conducting significant research in relevant computational science, such as algorithm creation and optimization, creation of appropriate languages, or the creation of hardware architectures applicable to the solution of biomedical problems; (2) conducting significant research and development in biomedical computational science by developing and deploying tools designed to solve particular biomedical problems; (3) establishing DBPs to allow experimental and clinical biomedical and behavioral researchers to interact with and drive computational research in the Center; (4) providing infrastructure to serve the needs of the broad community of biomedical and behavioral researchers; (5)

enhancing the training for a new generation of biomedical researchers in appropriate computational tools and techniques; (6) disseminating newly developed tools and techniques to the broader biomedical research community; and (7) providing an administrative Core to ensure that the large Center achieve its goals within the five to ten-year funding lifetime of the NIH NCBC.

Cores 1 and 2 in an NIH NCBC Center should propose research that is important to biomedical or behavioral researchers and interesting to researchers in computational biology. These Cores will be the largest component of a Center. The chosen research problem should be significant, but it should also be possible to achieve substantial progress in a five to ten-year timeframe. It is expected that the personnel associated with Core 1 will have a computer science or other mostly computational background. In contrast, it is likely that the personnel associated with Core 2 will have some computational background, but they will also have a significant background in some area of biomedical or behavioral research. Cores 1 and 2 do not have to be the same size, but both must exist. While no distribution of expenditures is prescribed for a Center, it is envisaged that Cores 1 and 2 together will comprise approximately half of the overall budget.

Close and effective collaboration between the leaders of Core 1 and Core 2 is key to the success of the NIH NCBC. The NIH NCBC will need cutting edge computer science, as represented by Core 1, and strong leadership in translating that computer science into effective algorithms and environments for solving real biological problems. Reviewers will evaluate applications for evidence of strong synergy between these two Cores in conceptualizing, planning, and implementing a Center. While it is not required that the leaders of Core 1 and Core 2 be at the same institution, applicants will have to present a convincing plan for any proposed collaboration at a distance.

In Core 3, an investigator will propose two to four collaborations with NIH funded biomedical or behavioral researchers to address a biomedical/behavioral question using computational approaches. It is not essential that the biomedical researchers have expertise in computational biology, but they must have a question that will drive the fundamental computational research in Cores 1 and 2. The purpose of this Core is to ensure that the research carried out in Cores 1 and 2 has direct relevance to biomedical or behavioral research. It may be useful for these DBPs to have a focus on a particular disease or organ, but that sort of focus might not be appropriate for all of the Centers. It is expected that many of the biomedical researchers in Core 3 will NOT be at the same institution as the parent Center. In such cases, convincing plans for collaboration at a distance must be presented in the application. An individual DBP will last for at most three years. If the problem addressed by the DBP is not going to be completely solved in a three-year period, the Principal Investigator and collaborating researchers must present plans to compete for independent funding for continuation of the work. Plans must also be presented to recruit and select additional DBPs when the initial “founding” DBPs under the Center have been completed. The plans for retiring and selecting new DBPs should be presented in Core 7. While no distribution of expenditures is mandated, it is envisaged that approximately one quarter of the budget in each Center will be used to support the participation of the DBPs. Funding for DBPs should be requested in all five years. The new DBPs in years 4 and 5 of the application will not be described in the application, so the presented budgets will be estimates based on the costs of the DBPs in years 1 through 3.

The new tools that are being developed are likely to require substantial infrastructure to allow the larger community of biomedical researchers to utilize these tools. Core 4 will provide that infrastructure. Examples of the infrastructure include user support personnel, servers from which users can download software or through which users can access the software on a national or regional facility, technical support to a national or regional facility on which users use the software, or related items to enable biomedical researchers to have ready access to the products of a Center.

The long-term goals of the NIH in bioinformatics and computational biology include the development of a new generation of multi-disciplinary biomedical computing scientists. In Core 5, each Center should propose specific and detailed plans to ensure that graduate students and postdoctoral fellows receive broad relevant training beyond the specific contributions they make to the infrastructure and research projects of the Center. This training should occur in both directions. Students and postdoctoral fellows with a background in computational science should receive training in biomedical and behavioral

science and those with a background in biomedical and behavioral science should receive training in computational sciences. In addition, plans should be presented for workshops or other activities to train the larger biomedical community about the new tools and techniques that the Center is developing. It may be most effective if some workshops occur in the context of important biomedical or behavioral science meetings, at universities or medical schools, or using resources such as the Access Grid rather than at the Center itself. The rationale for the structure and venue of the workshops should be carefully thought out and presented in the application.

The focus of Core 6 is to describe plans to disseminate discoveries, resources, software, and data to the biomedical community. Publications and a good web site are excellent ways to broadcast some of the discoveries of the Center, but those routes may not be sufficient to inform biomedical and behavioral investigators who require guidance in pursuing computational solutions to their questions. Innovative plans to disseminate discoveries to this biomedical community should be presented in Core 6. Applicants must also present their software dissemination plans in Core 6. They must describe how software will be made available to the general scientific community and justify any restrictions they might place on software dissemination. As part of the software dissemination plan, letters from appropriate institutional officials at all institutions participating in the Center will have to be included. Finally, plans to make data sets and databases available after funding for the Center has ceased should be presented.

It is essential to describe an appropriate administrative structure to manage the many facets of these large, complex Centers. This administrative plan should be presented as Core 7. In this section, specific plans should be included to integrate activities within and across Cores, and to interact with an external community who will be users of the tools created by the Center. Specific plans for selecting new DBPs should be described. Investigators are strongly encouraged to consider proposing a project manager for the Center. In addition to a project manager, it is expected that each Center will have an external advisory committee. This committee should meet at least on an annual basis to review progress and offer advice. Potential members of the external advisory committee must not be contacted until after an award has been made, and these members must not be listed in the application. Core 7 should also address how the Center will accommodate requests from individual investigators who want to make use of the Center via the anticipated individual investigator program announcements.

While no distribution of expenditures is mandated, it is anticipated that Cores 4, 5, 6, and 7 will together account for approximately one-quarter of the total budget of a Center. Taken together, Cores 4 through 7 enable each team to function as an integrated national Center.

Section II. Award Information

1. Mechanism of Support

This funding opportunity will use the U54 award mechanism. As an applicant, you will be solely responsible for planning, directing, and executing the proposed project.

This funding opportunity uses the just-in-time budget concepts. It also uses the non-modular budget format described in the PHS 398 application instructions. Specifically, a detailed categorical budget for the "Initial Budget Period" and the "Entire Proposed Period of Support" is to be submitted with the application.

The NIH (U54) is a cooperative agreement award mechanism. In the cooperative agreement mechanism, the Principal Investigator retains the primary responsibility and dominant role for planning, directing, and executing the proposed project, with NIH staff being substantially involved as a partner with the Principal Investigator, as described under the section VI. 2. Administrative and National Policy Requirements, "Cooperative Agreement Terms and Conditions of Award."

2. Funds Available

The participating ICs intend to commit $12-14 million dollars in FY 2005 to fund three new Centers in response to this RFA. An applicant may request a project period of up to five years and a budget for direct costs up to $2.6 million dollars in year 1, and may not exceed $2.7 million in subsequent years. These direct costs do not include the facilities and administration costs for subcontracts (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-040.html). Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size of each award will also vary. No Center will receive more than ten years total of NIH funding. Although the financial plans of the ICs provide support for this program, awards pursuant to this RFA are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

You may submit an application if your organization has any of the following characteristics:

- Public or private institutions, such as universities, colleges, hospitals, and laboratories
- Units of State and local governments
- Eligible agencies of the Federal government
- Domestic institutions/organizations
- Foreign institutions are not eligible to apply for an NIH NCBC Center, but foreign institutions can participate as subcontractors in any of the Cores

Academic-industry partnerships can be very useful for an NIH NCBC Center. For-profit organizations are not eligible to apply for a Center, but partnerships are welcome. Applicants who chose to include a for-profit organization should explain how the participation of that organization will affect the software dissemination and/or data sharing plans. For-profit organizations must meet the same criteria for software dissemination and data sharing as do academic researchers. For-profit organizations must adhere to the goals of the RFA and provide coherent letter to this effect by listing out all terms of agreement. This information should be placed in Core 6.

There is no limit on the number of applications from a single investigator or institution.

1.B. Eligible Individuals

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

The Principal Investigator of each Center must devote at least 25% of his/her effort.

2. Cost Sharing

This program does not require cost sharing as defined in the current NIH Grants Policy Statement at http://grants.nih.gov/grants/policy/nihgps_2003/nihgps_Part2.htm#matching_or_cost_sharing.

3. Other-Special Eligibility Criteria

None.

Section IV. Application Submission Instructions

1. Address to Request Application Information

The PHS 398 application instructions are available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY 301-451-0088.

2. Content and Form of Application Submission

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). Applications must have a D&B Data Universal Numbering System (DUNS) number as the universal identifier when applying for Federal grants or cooperative agreements. The D&B number can be obtained by calling (866) 705-5711 or through the web site at http://www.dnb.com/us/. The D&B number should be entered on line 11 of the face page of the PHS 398 form.

See also Subsection VI.2. for additional information.

The title and number of this funding opportunity must be typed on line 2 of the face page of the application form and the YES box must be checked.

3. Submission Dates and Time

3.A. Receipt, Review and Anticipated Start Dates

Technical Assistance Workshop: 10/28/2004
Letter of Intent Receipt Date: 12/20/2004
Application Receipt Date(s): 01/24/2005
Peer Review Date: April-June 2005
Council Review Date: August-September 2005
Earliest Anticipated Start Date: 09/15/2005

3.A.1. Letter of Intent

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Number and title of this funding opportunity

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed at the beginning of this document. It is preferable if the letter is sent by email.

The letter of intent should be sent to:

Kevin Lauderdale
Center for Bioinformatics and Computational Biology
National Institute of General Medical Sciences
45 Center Drive, Room 2AS55D, MSC 6200
Bethesda, MD 20892-6200
Telephone: 301-451-6446
FAX: 301-480-2802
Email: LauderdK@nigms.nih.gov

3.B. Sending an Application to the NIH

Applications must be prepared using the PHS 398 research grant application instructions and forms as described above. Submit a signed original of the application, including the checklist, appendix materials, and five signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710 (U.S. Postal Service Express or regular mail)
Bethesda, MD 20817 (for express/courier service; non-USPS service)

Using the RFA Label: The RFA label available in the PHS 398 application instructions must be affixed to the bottom of the face page of the application. Type the RFA number on the label. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked. The RFA label is also available at: http://grants.nih.gov/grants/funding/phs398/label-bk.pdf.

3.C. Application Processing

Applications must be received **on or before the application receipt date** listed in the heading of this funding opportunity. If an application is received after that date, it will be returned to the applicant without review.

The NIH will not accept any application in response to this funding opportunity that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. However, when a previously unfunded application, originally submitted as an investigator-initiated application, is to be submitted in response to a funding opportunity, it is to be prepared as a NEW application. That is, the application for the funding opportunity must not include an Introduction describing the changes and improvements made, and the text must not be marked to indicate the changes from the previous unfunded version of the application. However, applications that were submitted to RFA-RM-04-003 (originally RFA-RR-04-001) may be revised and resubmitted under this RFA. Revised applications must include an Introduction of not more than 10 pages that summarizes the substantial additions, deletions, and changes. The Introduction must also include responses to the criticisms and issues raised in the summary statement. The changes in the Research Plan must be clearly marked by appropriate bracketing, indenting, or changing of typography, unless the changes are so extensive as to include most of the text. This exception should be explained in the Introduction. Do not underline or shade changes. Acceptance of a revised application automatically withdraws the prior version, since two versions of the same application cannot be simultaneously pending.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within eight (8) weeks.

4. Intergovernmental Review

This initiative is not subject to intergovernmental review

5. Funding Restrictions

All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm (See also Section VI.3. Award Criteria)

6. Other Submission Requirements

The application for an NIH NCBC Center must include the following seven Cores: (1) conducting core research in computational science; (2) conducting core research applying computing to biomedical and behavioral problems; (3) establishing DBPs to allow biomedical and behavioral researchers to interact with and drive research in Cores 1 and 2; (4) providing infrastructure (hardware, software, and personnel as appropriate) to serve the needs of the broad community of biomedical researchers; (5) enhancing the training for a new field of biomedical researchers in appropriate computational tools and techniques; (6) disseminating newly developed tools and techniques to the broader biomedical research community; and (7) providing an administrative Core to ensure that these large Centers achieve their goals within the five to ten year funding lifetime of the Center.

It is recognized that the applications in response to this RFA will be longer and more complex than many other NIH applications. In order to ensure effective review, the Research plan should be divided into sections according to the above-defined Cores, and separate page limits should be observed for each section. It is not necessary to subdivide each of these Cores into the traditional a-d format specified in PHS 398, but this division may be useful for some Cores.

For Core 1 and Core 2, the computer science and computational science underlying the work of the proposed NIH NCBC Center, the combined total page limit is 90 pages. Cores 1 and 2 must not be combined into a single section. Applications that combine Cores 1 and 2 will be judged non-responsive and will be returned without review. Plans for the development of software for use by the biomedical community should have appropriate timelines and mileposts. Software development should include plans and timelines for alpha testing, beta testing, production release, interface development, bug reporting, integration with other codes, extension to multiple platforms, user support, etc. The software development plans should be presented in Core 2. The application should begin with an overview section that provides an executive summary of the application. This overview will be counted toward the 90 page limit.

For Core 3, the descriptions of the DBPs, the total page limit is 15 pages per DBP. This limit will be strictly enforced. If a DBP uses fewer than 15 pages, the extra pages may not be used in the description of another DBP. Since two through four DBPs are required, the page limits for this section are 30 to 60 pages.

For Cores 4 through 7, the page limit is 40 pages total. The software dissemination plan should be included in Core 6. The letters from appropriate institutional officials pledging support for the proposed dissemination plan should be included between Cores 6 and 7. Applicants should include a table of contents in front of these letters indicating the title of the person who wrote the letter and the institution that the letter came from. The letters section will not be counted toward the page limit, but the dissemination plan will be included in the 40-page limit.

Both reviewers and program staff appreciate brevity and clarity in the application. Page limits will be enforced, and it is anticipated that applications that do not adhere to the limits will be declared non-responsive and returned without review. Required information, in addition to that requested in the Form PHS 398 instructions, is listed below, by section. Applications that will involve human subjects or vertebrate animals must follow the rules in the PHS 398 instructions.

Budget: The budget should be completed as described in the instruction sheet for Application for a Public Health Service Grant (Form PHS 398). The budget section should begin with an overall budget for the Center using form pages 4 and 5. After these pages, form pages 4 and 5 should be prepared for Core 1, Core 2, Core 3, Core 4, Core 5, Core 6, and Core 7. Separate form pages 4 and 5 should be completed for each of the DBPs in Core 3. Each budget page should be clearly labeled. The budget justification should follow the budget for Core 7. This budget justification should include the justification for key personnel. As part of the justification, the percent effort that all staff spend on each Core should be specified. For example, a particular postdoctoral fellow might spend 75% effort on Core 1 and 25% effort on one DBP in Core 3. The Principal Investigator of each Center must devote at least 25% of his/her effort. A justification should be supplied for total equipment over $25,000 requested. Details of the physical location for such equipment should be provided. Similar existing equipment should also be described, and the need for the new equipment justified. Finally, form pages 4 and 5 should be provided for any sub-contractual or consortium arrangements. A detailed budget justification should also be provided for such arrangements.

Research Plan: Each of the seven Cores should be described. It will be best if the applicant uses separate headings for each of these Cores. Cores 1 (conducting core research in computing), 2 (conducting core research applying computing to biomedical problems), and 3 (establishing Driving Biological Projects) should be broken into appropriate subheadings.

When developing the application, the applicant should be aware of the following points.

The annual progress report for the U54 award will use the standard 2590 form as well as supplementary information that will be more extensive. Additional information in the progress report will include both the progress made in the Center as well as the relationship between the Center and collaborators. Details of the U54 progress report are spelled out in the Notice of Grant Award and in Section VI.4 of this RFA. Applications for U54 Centers should request appropriate personnel to collect the needed information and to prepare this progress report.

Because of the complexity of the NIH NCBC, program staff from NIH will likely conduct periodic administrative site visits. U54 Centers should be prepared for an annual site visit and an annual all-hands NIH NCBC meeting, and this should be included in the budget (including travel for collaborators and other necessary costs).

Each Center application is expected to include a well-developed management plan. If appropriate, the management plan should include provisions for teleconferencing or videoconferencing.

The complexity of these Centers suggests that it may be necessary to request a project manager. The U54 Centers should budget appropriately for this manager. One of the review criteria for these Centers will be the qualifications of this project manager as well as whether the institution has an appropriate career pathway for this individual. Because of this important role, it is recommended that a project manager be listed as one of the key personnel.

Appendix: No more than 10 publications can be included in the appendix.

Applicants should not contact members of the proposed Center's external advisory committee prior to award. Applicants should not name members of the proposed Center's external advisory committee in the application.

Plan for Sharing Research Data

The precise content of the data-sharing plan will vary, depending on the data being collected and how the investigator is planning to share the data. Applicants who are planning to share data may wish to describe briefly the expected schedule for data sharing, the format of the final dataset, the documentation to be provided, whether or not any analytic tools also will be provided, whether or not a data-sharing agreement will be required and, if so, a brief description of such an agreement (including the criteria for deciding who can receive the data and whether or not any conditions will be placed on their use), and the mode of data sharing (e.g., under their own auspices by mailing a disk or posting data on their institutional or personal website, through a data archive or enclave). Investigators choosing to share under their own auspices may wish to enter into a data-sharing agreement. References to data sharing may also be appropriate in other sections of the application.

All applicants must include a **plan** for sharing research data in their application. The data sharing policy is available at http://grants.nih.gov/grants/policy/data_sharing. All investigators responding to this funding opportunity should include a description of how final research data will be shared, or explain why data sharing is not possible. The reasonableness of the data sharing **plan** or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data sharing **plan** into the determination of scientific merit or the priority score.

Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication. NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm and http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc54600131. Investigators responding to this funding opportunity should include a **plan** for sharing research resources addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the resources sharing **plan** and the related data sharing **plan** will be considered by Program staff of the funding organization when making recommendations about funding applications. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report. (PHS 2590). See Section VI.3. Award Criteria.

Plans for the development of research resources for use by the biomedical community should have appropriate timelines and mileposts. Core 6 is the best place for timelines and mileposts relating to resources.

Plan for Sharing Software

A software dissemination plan, with appropriate timelines, must be included in Core 6 of the application. There is no prescribed single license for software produced in this project. However, NIH does have goals for software dissemination, and reviewers will be instructed to evaluate the dissemination plan relative to these goals:

1. The software should be freely available to biomedical researchers and educators in the non-profit sector, such as institutions of education, research institutions, and government laboratories.
2. The terms of software availability should permit the commercialization of enhanced or customized versions of the software, or incorporation of the software or pieces of it into other software packages.
3. The terms of software availability should include the ability of researchers outside the Center and its collaborating projects to modify the source code and to share modifications with other colleagues as well as with the Center. A Center should take responsibility for creating the original and subsequent “official” versions of a piece of software, and should provide a plan to manage the dissemination or adoption of improvements or customizations of that software by

others. This plan should include a method to distribute other user's contributions such as extensions, compatible modules, or plug-ins.

The application MUST include written statements from the officials responsible for intellectual property issues at all of the applicant institutions (including sub-contractors), to the effect that the institution supports and agrees to abide by the software dissemination plans put forth in the application. These letters must be clear expressions of commitment. A separate letter should be sent by each participating organization including each subcontractor. Lack of such letters will result in withdrawing the application as non-responsive. These letters should be placed between Cores 6 and 7 and should include a table of contents as described above.

Additionally, peer reviewers, program staff, and advisors will evaluate the adequacy of dissemination plans prior to award (see below). Please note that institutional sign-off on the grant application signifies that all relevant components of the institution, including the technology transfer office, have reviewed and approved the document.

The initial review group will comment on the appropriateness of the proposed plan for data and materials dissemination. Program staff and advisors will also consider the adequacy of the dissemination plan as one of the criteria for award. The proposed sharing plan, after negotiation with the applicant when necessary, will be made a condition of the award. Evaluation of competing renewal application and annual non-competing progress reports will include assessment of the responsiveness to NIH guidelines of data, materials, methods, and software dissemination practice by the grantee.

Section V. Application Review Information

1. Criteria

Adminstrative Criteria: Upon receipt, applications will be reviewed for completeness by the CSR and responsiveness by NIGMS. Incomplete applications will not be reviewed.

If the applications are not responsive to the RFA, NIH staff may contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the appropriate review cycle.

2. Review and Selection Process

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by NIGMS in accordance with the review criteria stated below.

As part of the initial merit review, all applications will:

- Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score.
- Receive a written critique
- Receive a second level of review by the National Advisory General Medical Sciences Council

3. Merit Review Criteria

Applications submitted in response to a funding opportunity will compete for available funds with all other recommended applications.

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. The scientific review group will address and consider each of these criteria in assigning the application's overall score, weighting them as appropriate for each application.

- Significance
- Approach
- Innovation
- Investigator
- Environment
- Additional Review Criteria

The application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

Significance: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field? Evaluate how the computational and biological problems proposed by the NIH NCBC Center make it national in scope.

Approach: Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

Innovation: Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

Investigator: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the Principal Investigator and other researchers (if any)?

Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

3.A. Additional Review Criteria:

In addition to the above criteria, the following items will be considered in the determination of scientific merit and the priority score:

Investigators are strongly encouraged to address the following elements, and reviewers will be asked to assess these elements in their critiques.

Review Criteria Relating to Cores:

Cores 1-3: Will the work proposed in these Cores help establish an integrated national biomedical computing environment? Is the proposed work essential to establishing this environment? Is there evidence of an effective approach to managing the interactions between the software engineering parts of the Center (in Cores 1 and 2) and the biological problems coming from Core 3? Will the

software engineering plans (timelines, plans for version control, bug reporting...) provide robust software for the user community?

Core 3: Do the investigators have appropriate plans to obtain support for the DBPs after their support from the Center has terminated? Do the DBPs drive the work proposed in Cores 1 and 2? Evaluate how the proposed DBPs in concert with Cores 1 and 2 make the Center national in scope.

Core 4: Are the infrastructure requests adequate to meet the demands that are likely to come from biomedical or behavioral researchers?

Core 5: Will the proposed training help create a new group of multi-disciplinary or interdisciplinary investigators? Are the training plans sufficiently detailed and innovative? Evaluate how the proposed training makes the Center national in scope.

Core 6: Are the plans for dissemination of discoveries adequate? Evaluate how the plans for dissemination make the Center national in scope.

Software Sharing Plan: Reviewers will be asked to assess: the adequacy of milestones for software dissemination; whether the plan for sharing and distributing the software allows wide and easy access; the appropriateness of any fee structures; and the plans and methods for ensuring interoperability of data and software. Reviewers are asked to factor the proposed software sharing plan into the determination of scientific merit and the priority score for Core 6.

The adequacy of the software sharing plan will be considered by Program staff when making recommendations about funding applications. Program staff may negotiate modifications of the software sharing plan with the Principal Investigator before recommending funding of an application. The final version of the software sharing plan negotiated by both will become a condition of the award of the grant. The effectiveness of the software sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report. (PHS 2590). See Section VI.3. Award Criteria.

Core 7: Will the proposed management structure allow the Center to achieve its goals? Does the institution have an appropriate career path for the project manager? Is the mechanism to terminate old DBPs and choose new ones adequate? Are the plans to incorporate individual investigator awards likely to work?

Reviewers should consider all seven components of the project as important, even if a particular component represents only a relatively small part of the budget. For example outreach and training, while not as costly as the core development of the computational environment, is considered to be critically important for the NIH NCBC to have the appropriate impact on biomedical research.

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed. See also Section VIII - Other Information.

Inclusion of Women, Minorities and Children in Research: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated. See also Section VIII-Other Information.

Care and Use of Vertebrate Animals in Research: If vertebrate animals are to be used in the project, the five items described under Section f of the PHS 398 research grant application instructions (rev. 5/2001) will be assessed.

3.B. Additional Review Considerations

Budget: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

3.C. Sharing Research Data

Data Sharing Plan: The reasonableness of the data sharing **plan** or the rationale for not sharing research data **will** be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score. The presence of a data sharing **plan** will be part of the terms and conditions of the award. The funding organization will be responsible for monitoring the data sharing policy.

3.D. Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication. NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps and http://ott.od.nih.gov/newpages/rtguide_final.html. Investigators responding to this funding opportunity should include a sharing research resources **plan** addressing how unique research resources will be shared or explain why sharing is not possible. The reasonableness of the resources sharing **plan** or the rationale for not sharing research resources **will** be assessed by the reviewers. However, reviewers will not factor the proposed resource sharing plan into the determination of scientific merit or the priority score.

The adequacy of the resources sharing **plan** will be considered by Program staff of the funding organization when making recommendations about funding applications. Program staff may negotiate modifications of the data and resource sharing **plans** with the Principal Investigator before recommending funding of an application. The final version of the data and resource sharing **plans** negotiated by both will become a condition of the award of the grant. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report. (PHS 2590). See Section VI.3. Award Criteria.

Section VI. Award Administration Information

1. Award Notices

After the peer review of the application is completed, the Principal Investigator will also receive a written critique called a summary statement.

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant. For details, applicants may refer to the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part4.htm

A formal notification in the form of a Notice of award will be provided to the applicant organization. The notice of award signed by the grants management officer is the authorizing document.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NGA (Notice of Grant Award) are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs.

An award notice will be sent via email to the institution’s business official.

2. Administrative and National Policy Requirements

All NIH Grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the notice of grant award. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part4.htm and Part II Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part9.htm.

The following Terms and Conditions will be incorporated into the award statement and will be provided to the Principal Investigator as well as to the appropriate institutional official, at the time of award.

2.A. Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable OMB administrative guidelines, HHS grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement (U54, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

Failure of the awardees to meet the performance requirements, including these special terms and conditions of award, or significant changes in level of performance, may result in a reduction of budget, withholding of support, suspension and/or termination of the awards.

2.A.1. Principal Investigator Rights and Responsibilities

The Principal Investigator will have the primary responsibility to define objectives and approaches of the Center, and to plan, conduct, analyze, and publish results, interpretations, and conclusions of the studies. The primary responsibilities of the awardees are to:

- Define the research objectives.
- Conduct specific studies.
- Analyze and interpret research data.
- Establish an external advisory committee for the Center.
- Provide information to the NIH Science Officer and NIH Program Officer concerning progress.
- Maintain career development opportunities to encourage new investigators to work in computational biology.

Awardees will retain custody of and primary rights to their data and intellectual property developed under the award subject to current government policies regarding rights of access as consistent with current HHS, PHS, and NIH policies and subject to the terms and conditions of this RFA.

Principal investigators and key personnel as appropriate are expected to participate in an annual meeting all-hands NIH NCBC meeting, and to host an annual site visit.

Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.

2.A.2. NIH Responsibilities

NIH Science Officers will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below. NIH Science Officers will be NIH staff who will have substantial scientific involvement during the conduct of this activity, through technical assistance, advice, and coordination above and beyond normal program stewardship for grants. Each Center will have one or more designated NIH Science Officer(s). A given individual may be the NIH Science Officer for more than one Center. The degree of involvement by the NIH Science Officer(s) will include the following:

- Assist in avoiding unwarranted duplication of effort across the NIH NCBC; help coordinate collaborative research efforts that involve multiple Centers.
- Review and comment on critical stages in the research program before subsequent stages are implemented.
- Assist in the interaction between the awardee and investigators at other institutions.
- Retain the option of recommending termination of studies if technical performance falls below acceptable standards, or when specific lines of research cannot be effectively pursued in a timely manner.
- Retain the option to recommend additional research endeavors within the constraints of the approved research and negotiated budget.

To help carry out these duties, Science Officers may consult with non-NIH experts in the field.

Additionally, an agency program official or IC program director will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice. This individual will not be a Science Officer. The Program Officer will:

- Have the option to recommend withholding support to a participating institution if technical performance requirements are not met.
- Exercise the normal stewardship responsibilities of an NIH Program Officer.
- Carry out continuous review of all activities to ensure objectives are being met.

2.A.3 Collaborative Responsibilities

None.

2.A.4. Arbitration Process

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to arbitration. An Arbitration Panel composed of three members will be convened. It will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special arbitration procedure in no way affects the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulations 42 CFR Part 50, Subpart D and HHS regulations 45 CFR Part 16.

3. Award Criteria

The following will be considered in making funding decisions:

- Scientific merit of the proposed project as determined by peer review
- Availability of funds
- Relevance of program priorities

- Complementarity with existing NIH NCBC Centers

4. Reporting

Awardees will be required to submit the PHS Non-Competing Grant Progress Report, Form 2590 annually:
http://grants.nih.gov/grants/funding/2590/2590.htm and financial statements as required in the NIH Grants Policy Statement.

The progress of each NIH NCBC Center will be reviewed annually by the NIH Program Officer to assure that satisfactory progress is being made in achieving the project objectives. During the first year of funding, and during subsequent years if deemed necessary by the Program Officer, reviews may be more frequent. Should problems arise in the conduct of the study, the NIH Program Officer may require that the awardee submit quarterly reports on progress and fiscal matters.

The annual progress report will have two components. The first will be the standard NIH progress report (Form 2590) described above. The second will be a more specialized report that will go to the NIH Science Officer(s) and the NIH Program Officer. This specialized report should be included as an attachment to the standard progress report. The report will contain a narrative section describing the progress in each of the seven Cores over the past year. The report will also contain at least two "highlights." Each highlight will be based on a publication or other product of the Center, less than a year old, which acknowledges support from the National Institutes of Health NCBC. The highlight will be written at a level that is understandable by a technically literate, but non-expert individual. The report will also contain details of the federally funded investigators that used the resources in the Center during the preceding fiscal year. The report will also contain a list of papers that acknowledge support from the NIH NCBC as well as publications that used the Center but did not acknowledge support. These two lists of publications will be presented separately.

Section VII. Agency Contacts

We encourage your inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues:

1. Scientific/Research Contacts:

John Whitmarsh, Ph.D.
Program Officer
Center for Bioinformatics and Computational Biology
National Institute of General Medical Sciences
45 Center Drive, Room 2AS 55F, MSC 6200
Bethesda, MD 20892-6200
Telephone: (301) 451-6446
FAX: (301) 480-2802
Email: whitmarj@nigms.nih.gov

Peter Lyster, Ph.D.
Program Officer
Center for Bioinformatics and Computational Biology
National Institute of General Medical Sciences
45 Center Drive, Room 2AS 55K, MSC 6200
Bethesda, MD 20892-6200
Telephone: (301) 451-6446

FAX: (301) 480-2802
Email: lysterp@nigms.nih.gov

2. Peer Review Contacts:

Sally Amero, Ph.D.
Chief, Bioengineering Sciences and Technology IRG
Center for Scientific Review
6701 Rockledge Drive, Room 4190, MSC 7826
Bethesda, MD 20892-7826
Telephone: (301) 435-1159
FAX: 301-480-4042
Email: ameros@csr.nih.gov

3. Financial or Grants Management Contacts:

Antoinette Holland
Grants Administration Branch
National Institute of General Medical Sciences
45 Center Drive, Room 2AN 50B, MSC 6200
Bethesda, MD 20892-6200
Phone: (301) 594-5132
Fax: (301) 480-2554
hollanda@nigms.nih.gov

Section VIII. Other Information

Required Federal Citations

Use of Animals in Research:
Recipients of PHS support for activated involving live, vertebrate animals must comply with PHS Policy on Humane Care and Use of Laboratory Animals (http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf), as mandated by the Health Research Extension Act of 1985 (http://grants.nih.gov/grants/olaw/references/hrea1985.htm), and the USDA Animal Welfare Regulations (http://www.nal.usda.gov/awic/legislat/usdaleg1.htm), as applicable.

Human Subjects Protection:
Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm.

Data and Safety Monitoring Plan:
Data and safety monitoring is required for all types of clinical trials, including physiologic toxicity, and dose-finding studies (phase I); efficacy studies (Phase II) efficacy, effectiveness and comparative trials (Phase III). Monitoring should be commensurate with risk. The establishment of data and safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risks to the participants. (NIH Policy for Data and Safety Monitoring, NIH Guide for Grants and Contracts, June 12, 1998: http://grants.nih.gov/grants/guide/notice-files/not98-084.html).

Sharing Research Data:
Investigators submitting an NIH application seeking $500,000 or more in direct costs in any single year

are expected to include a plan for data sharing or state why this is not possible. http://grants.nih.gov/grants/policy/data_sharing

Investigators should seek guidance from their institutions, on issues related to institutional policies, local IRB rules, as well as local, State and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

Sharing of Model Organisms:
NIH is committed to support efforts that encourage sharing of important research resources including the sharing of model organisms for biomedical research (see http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html). At the same time the NIH recognizes the rights of grantees and contractors to elect and retain title to subject inventions developed with Federal funding pursuant to the Bayh Dole Act (see the NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm). All investigators submitting an NIH application or contract proposal beginning with the October 1, 2004 receipt date, are expected to include in the application/proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding or state why such sharing is restricted or not possible. This will permit other researchers to benefit from the resources developed with public funding. The inclusion of a model organism sharing plan is not subject to a cost threshold in any year and is expected to be included in all applications where the development of model organisms is anticipated.

Inclusion of Women And Minorities in Clinical Research:
It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43). All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

Inclusion of Children as Participants in Clinical Research:
The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all clinical research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at http://grants.nih.gov/grants/funding/children/children.htm.

Required Education on The Protection of Human Subject Participants:
NIH policy requires education on the protection of human subject participants for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. The policy is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

Human Embryonic Stem Cells (hESC):
Criteria for federal funding of research on hESCs can be found at http://stemcells.nih.gov/index.asp and at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (see http://escr.nih.gov/) It is the responsibility of the applicant to provide in the project description and elsewhere in the application as appropriate, the official NIH identifier(s) for the hESC line(s)to be used in the proposed research. Applications that do not provide this information will be returned without review.

Public Access to Research Data through the Freedom of Information Act:
The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm. Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

Standards for Privacy of Individually Identifiable Health Information:
The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information", the "Privacy Rule", on August 14, 2002 . The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR).
Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

URLs in NIH Grant Applications or Appendices:
All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

Healthy People 2010:
The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople.

Authority and Regulations:
This program is described in the Catalog of Federal Domestic Assistance at http://www.cfda.gov/ and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles,

and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Weekly TOC for this Announcement
NIH Funding Opportunities and Notices

Department of Health
and Human Services

National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

In the News

NIH Director's Pioneer Award

First NIH Director's Pioneer Award Recipients Named

- NIH Director's Pioneer Award overview
- Pioneer Award Recipient bios
- More information

- More Press Releases...

Health Issues

- Menopausal Hormone Therapy

Medical Research Issues

- Public Access
- NIH Roadmap
- HIPAA Privacy Rule
- Stem Cell Information
- Conflict of Interest Information

Health Information

A-Z index of NIH health resources, clinical trials, health hotlines, MEDLINEplus, drug information

Grants & Funding Opportunities

Grants news, applications, grants policy, NIH Guide, award data, research training, research contracts, loan repayment programs, Small Business Research Programs

News & Events

Press releases, media center, calendars, radio & video, media contacts

Scientific Resources

Human Embryonic Stem Cell Registry, intramural research, special interest groups, library catalogs, journals, training, labs, scientific computing

Institutes, Centers & Offices

The individual organizations that make up the NIH

About NIH

Visitor info, jobs, science education, employee directory, public involvement, policy issues, organization & mission, history, doing business with NIH, FOIA, Director's Page

Q&A About NIH

Career Opportunities

Visitor Information

Employee Information

Información en español

Featured this week

The Promise of Personalized Medicine

Medical Investigation on TV: Facts about

- Genetic Disorders
- Infertility

National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892

Department of Health and Human Services

FIRSTGOV
Your First Click to the U.S. Government